Remarks

Claims 1-9, 12 and 13 were pending. Claim 1 is amended. Support for the amending language may be found in the specification, in the summary of the invention, and paragraph 11, line 8.

Claim 1 has been objected to, and rejected under 35 U.S.C. 112. Applicants have deleted the noted typographical error. Withdrawal of the objection and rejection is requested.

Claims 1, 2, 7 and 8 have been rejected under 35 U.S.C. 102(b) as anticipated by Clay *et al.* (2001) and/or obvious under 35 U.S.C. 103(a). Applicants respectfully submit that the presently claimed invention is not anticipated or suggested by the cited art.

The present claims have been amended to recite a cell that exclusively gives rise to megakaryocytes and progenitors.

As discussed in the specification at paragraphs 85-92, the inventors prospectively searched for cells that could give rise to <u>only</u> megakaryocytes and extensively tested their differentiation potentials in several *in vitro* and *in vivo* assays. The MKPs isolated here meet all criteria for megakaryocyte-committed progenitors and therefore provide a definitive proof of the existence of these monopotent progenitors.

The cells isolated by Clay *et al.* differ from the presently claimed cells in their cell surface phenotype and in their developmental potential. Applicants note that the present claims have been amended to recite a lineage panel, which lineage panel was not used for selection in the cited prior art reference.

On page 1985 of Clay et al., it is stated that "in some experiments, $CD9^{+}CD41^{+}$ cells were sorted according to CD41 expression; gates D and C (Figure 3) corresponded to $CD41^{mid/low}$ and $CD41^{high}$ cells, respectively."

Clay *et al.* analyzed the sorted cells as follows:

> In contrast to the other myeloid progenitors, when $CD34^{+}CD41^{-}$ bone marrow cells were sorted into $CD9^{low}$, $CD9^{mid}$, and $CD9^{high}$ subpopulations, CFU-MK were highly enriched in the $CD9^{high}$ population (Figures 4, 5). Only a small proportion of CFU-MK was detected in the $CD9^{low}$ fraction, and an intermediate proportion was detected in the $CD9^{mid}$ fraction. As indicated earlier, a small fraction of the $CD34^{+}CD9^{+}$ cells expresses the CD41 antigen. <u>Therefore, we sorted $CD9^{high}$ and $CD9_{mid}$ cells according to their CD41 expression level (Figure 3). The proportion of CFU-MK was 4-fold higher in the $CD9^{mid}CD41^{neg}$ fraction (gate B) than in the $CD9^{mid}CD41^{mid/low}$ population (gate D) (24 ± 2 and 6 ± 1, respectively, for 10_4 plated cells). In contrast, $CD9^{high}CD41^{high}$ (gate E) only gave rise to a small number of differentiated megakaryocytic clusters.</u>

When EPO was added to these cultures, BFU-E/MK mainly arose from the differentiation of the $CD9^{mid}$ cells (21 ± 16 for 10^4 plated cells) compared to $CD9^{high}$ (7 ± 4 for 10^4 plated cells). Few BFU-E/MK were detected in the $CD9^{low}$ fraction and even then only in some experiments (data not shown).

One of skill in the art will conclude from the teachings of Clay *et al.* that the cell population of $CD34^+CD41^+CD9^+$ cells that are unsorted for lineage markers comprises progenitor cells for mixed erythroid colonies (BFU-E/MK), and therefore is not a population that gives rise exclusively to megakaryocytes and platelets.

Applicants therefore submit that the phenotypic and functional characterization of the prior art cell population differs from the characteristics of the presently claimed cell population. One of skill in the art would not be motivated to pursue a monopotent megakaryocyte progenitor cell in the cell populations defined by Clay *et al.*, as the $CD34^+CD41^+CD9^+$ population was stated to contain only a small number of differentiated megakaryocyte clusters.

An analysis of Clay et al. is also provided in the attached Declaration under 37 C.F.R. 1.132, by Dr. Holger Karsunky.

In view of the above amendments, remarks, and Declaration, withdrawal of the rejection is requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number STAN-278.

Respectfully submitted,
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